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VOLUME II

YELLOW FEVER : ITS TRANSMISSION BY MEANS
OF THE CULEX MOSQUITO

Charles FINLAY

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BALTIMORE, MARYLAND
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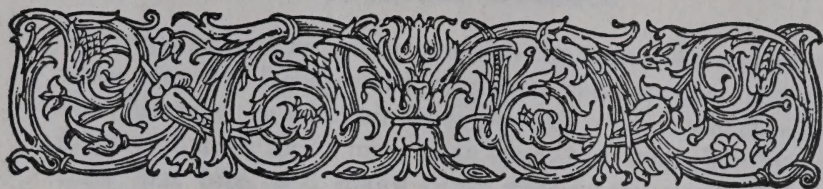
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Yellow Fever: Its Transmission by Means of the Culex Mosquito

BY

CHARLES FINLAY, M.D.

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IN THE month of May, of last year, when the yellow fever epidemic was commencing at Vera Cruz, Dr. Carmona, of Mexico, inoculated six prisoners with the dried residue of yellow fever urine. In two of the six, the local symptoms of the inoculation were immediately followed by those of fatal yellow fever, and, a few days later, both died *on the same day* (Carmona, *Leçons sur l'étiologie et la prophylaxie de la fièvre jaune*, p. 265). This unfortunate result agrees with the views I have entertained since 1881, viz., that whereas the disease is not spontaneously transmissible by infection through the air nor by contact, it can be communicated by inoculation. In searching for a natural agent capable of fulfilling this condition, I was led to fix upon the Culex mosquito as the most likely one. Before submitting, however, the experimental results which, so far, appear to confirm my theory, it will be necessary to describe the habits and peculiarities of this insect.

Most books on natural history inform us that only the *female* mosquito stings human beings and animals for the purpose of sucking their blood, the *males* feeding only on sweet juices or nutrient liquids. The fecundated females, in cold climates, hibernate during winter, in a state of apparent death, in dark

corners, in cellars, etc., to revive with the return of warm weather, when they will lay eggs and propagate their species. I was unable, however, to ascertain from previous writers whether gnats, in general, suck blood more than once, how long they live after their first bite, and many other particulars essential for my investigation. I was, therefore, obliged to undertake a systematic study of the species generally found in Havana, to which alone the following remarks must be understood to apply, leaving future inquiries to determine (p. 396) whether the same may be true of others that are known to exist in the interior of the island and in foreign countries.

Two species of mosquitoes are commonly observed in Havana. One, the *Culex cubensis* (La Sagra), *zancudo*, or long-legged mosquito, is from five to six mm. in length, of a yellowish or fawn color, with long, thin legs, and no noticeable spots upon its body or legs. This species is nocturnal, coming out exclusively at night and retiring before daybreak; they are often found in the morning, in a state of torpor, gorged with blood, inside of mosquito nets. I have never succeeded in getting these *zancudos* to sting a second time after they had once become filled; but as they can be kept alive, by feeding with sugar, over a period of forty days, it is unlikely that they should not bite more than once when in a state of freedom. The female of this species lays its eggs pretty much in the same manner as the European gnat, described by Reaumur, forming a boat-like aggregate of eggs, where over one hundred are closely packed together, standing upright, side by side, the tiny raft being left floating upon the water.

The other species is the *Culex* mosquito (Robineau Desvoidy), lately described, I am told, as "*Culex fasciatus*." There are several varieties, principally distinguishable by their dimensions and shades of color; some being small and nearly black, while others are stronger, almost as large as the nocturnal species, and of a brown or steel color; the general characteristics being the same in the two or three varieties that I have observed.

The body of the *C. mosquito* is dark colored, the ventral surface coated with a thick skin and marked with gray or white rings; on each side of the abdomen is a double row of white dots,

between which stretches a transparent membrane through which the blood can be seen when the insect is full. The most striking feature consists in five white rings on its hind legs, corresponding to the tarsal and metatarsal articulations. Others less apparent are on the fore and middle legs; white spots are visible on the sides of the thorax and front of the head, while the corselet presents a combination of white lines in the figure of a two-stringed lyre. The wings, when closed, do not cover the end of the body.

The *males* are known by their bushy antennae and long palps lying close to the proboscis, and curved outward near the point; whereas the *females* have delicate antennae and short palps drawn up close to the root of the proboscis.

The female of this species lays its eggs in a different manner from the *zancudo*, not in a boat-like aggregate but singly, having previously deposited a viscous substance through which they lie scattered in irregular groups, either upon the liquid surface or upon the sides of the vessel, close to the water's edge.

The above details are easily made out with the aid of a magnifying (p. 397) glass. I need not enter upon a minute description of the six pieces which constitute the sting of the female mosquito (labrum, mandibles, maxillae, and tongue); suffice it to say that, in the act of biting¹ and sucking blood it represents a hollow lance, from 2 to 2½ mm. long, 1/30 mm. broad at its base and about 1/40 near its extremity. The point is shaped like that of a writing pen, its edges being provided with ten or twelve sharp teeth decreasing in size as they reach the finely pointed extremity. The shaft presents transverse serrated ridges, which must act somewhat like the teeth of a conical file; these ridges, as well as the terminal teeth, belonging to the mandibles which are closely applied upon the sides of the labrum.

The sting remains enclosed in a brown, hairy sheath, excepting when it is introduced into the skin; during this operation, the sheath, which is slit in front to within a short distance of its point, bends backward and the sting appears like a fine wiry lance. This generally penetrates to a depth of from 1½ to 2 mm. before a

¹ This term is used in accordance with general custom notwithstanding its obvious inaccuracy.

bloodvessel is reached of sufficient calibre to allow blood to be drawn. The insect requires from one to five or seven minutes to complete this operation. When once it has fairly implanted its sting, the mosquito can be easily covered with a glass tube or phial and imprisoned. I have generally resorted to this means in order to procure live specimens, so as to be sure of their efficacy for my experiments.

The *C. mosquito* is diurnal and crepuscular, making its appearance early in the morning, again between 9 and 10 a. m., and in the afternoon until night. Stragglers may be met as late as 10 or 11 p.m., and in close, dark rooms they are generally felt or heard throughout the day (in summer). The males are the first to make their appearance, apparently attracted by the emanations of human perspiration from the body or from worn clothes; they keep flying about until the females appear, and it is only after pairing that the new females are able to sting and draw blood. When caught as they emerge from their pupa-case, they often attempt to do so, but their proboscis bends, either from want of rigidity of the sheath, or from obstruction at its point, and the lance fails to pierce the skin. Immediately after pairing, however, the insect is ready to sting.

I have found no difficulty in getting this species to do so as often as it has completed the digestion of the blood previously sucked, but not before an interval of from two to five days (according to the season and the weather), when the insect had been able to fill itself completely. As a proof of the remarkable resistance of this insect to rough usage, and in order to exemplify some of its habits, I copy the following record from my notebook:

(p. 398) *January 13, 1881.* A fresh female *C. mosquito* was caught in the afternoon and allowed to fill with blood off my hand, being retained captive in a glass tube closed with a muslin cap.

15th. Filled again from my hand, biting through the muslin cover.

16th. Strong and active; still distended with blood, refuses to sting.

17th. Stings my hand readily through the muslin and fills.

18th. Though still retaining some blood, bites my hand readily through the muslin. Two hours later, not having apparently taken its usual quantity of blood at the previous bite, it stings again and sucks during two minutes. (Probably the interposition of the muslin interferes with the act of sucking.) At this period, knowing that only the fecundated females draw blood, I introduced a small quantity of water into the phial, in order that eggs might be laid. The insect immediately goes to the water, and after discharging a whitish viscid substance upon the sides of the tube, deposits some white eggs, close to the edge of the water. Six of them were disposed vertically one above the other. The rest of the day the insect was busy besmearing every part of its body (legs, wings, and head included) with a viscid substance collected with the hind legs from the posterior extremity of the body. The white eggs turned black after some hours.

19th. Continues laying eggs.

20th. More eggs; some upon the sides of the phial; stings my hand and sucks readily. The water becomes colored red from the excrementitious particles discharged into it.

21st. Refuses to sting; has lost its left hind leg.

22d. Still laying. One small wriggler has been hatched. Cannot be got to sting.

23d. More eggs laid. Refuses to sting.

24th. The water is teeming with wrigglers. The insect was now transferred to another phial with water. Stings my bare hand very readily, taking about seven and a half minutes to fill.

25th. Refuses to sting. No new eggs.

26th. Bites readily, but, unable to reach a bloodvessel, withdraws its sting, and after feeling the surface of the skin, finds a more convenient spot, where it fills completely.

27th. Refuses to sting. In moving the phial the insect was soaked by the water, but recovered.

28th. Has laid over fifty eggs since yesterday evening; bites readily, and fills from my hand.

29th. Refuses to sting. No new eggs. Most of the white marks upon the body of the mosquito have nearly disappeared.

31st. Bites readily, and fills from the palm of my hand.

February 2. Bites, and fills from my thumb. Having been transferred to another phial with fresh water, was found lying partly submerged and motionless. On filtering off the water the insect revived. It was then transferred to a new dry phial for the purpose of continuing the observations during my trip to New York.

3d. Still retains some black blood; has lost its left foreleg.

4th. Bites, and fills from my hand. Taken on board of the steamer starting for New York.

5th. Refuses to sting.

6th. Bites, and fills readily.

(p. 399) *7th, 8th, 9th, 10th.* Alive, but refuses to sting. The weather was quite cold, the last three days passed off Sandy Hook.

12th. The phial, packed in a valise, was sent by express to Orange, N. J.; the insect arrived nearly dead.

13th. Dead, after thirty-one days captivity, having bitten twelve times, and laid probably over two hundred eggs.

From inquiries made on the steamer, I ascertained that mosquitoes are rarely felt on board during the three or four days that the vessel is detained in the port of Havana, where she lies at a distance from the wharves. In New York, where the ship goes to the wharf, they are apt to be more troublesome, but generally disappear soon after the vessel has left the port.

Mosquitoes are observed in Havana all the year through, but much more so from May to October. In winter they are rare when the temperature falls below 70° F. Last year (1885) has been an exception to the general rule. Mosquitoes, especially the diurnal species, were difficult to procure throughout the summer; but became more numerous in the latter part of September, October, and November. A remarkable scarcity of yellow fever cases was likewise observed in the summer months, and I called attention to this coincidence at one of the sessions of our Academy. In October and November more cases of the disease were signalled, both in hospital and private practice, than in the previous months of the year, although the summer heat had been

more intense than usual, and had abated toward the end of September, in October and November the weather being quite mild.

Although great differences are observed in the duration of the successive phases of development of the *C. mosquito*, the following data may be taken as a fair average: Every mosquito that stings may be considered as a fecundated female, and will probably lay eggs within a few days after its bite, provided it can find water upon which to lay them. In water-jugs standing in bedrooms, the insect is often found depositing its eggs either on the sides of the jug or upon the water. The eggs are commonly hatched, producing minute wrigglers, between the second and fourth day, in summer; some are delayed much longer, and those that are deposited outside the water may remain a long time in the dry state without losing their vitality. The wrigglers grow more or less rapidly according to the nutritive material contained in the water, the temperature, etc., but they probably pass into the pupa stage within twelve or fourteen days. This stage is always short, not lasting more than two or three days, the fully developed mosquito emerging from its aquatic case a fortnight or three weeks after the egg was laid.

From the above data it will be understood how a single infected mosquito, which happens to be conveyed to a healthy locality, when the temperature and altitude are appropriate, might, if my theory be true, (p. 400) inoculate the disease to any liable subject whom it should there sting; and, according to the usual rate of incubation, at the end of a fortnight or three weeks, the consequent attack of yellow fever would be at its height. In the meantime the imported insect would have produced a whole brood of its own species, probably in the vicinity of the place where the patient is lying; thus providing the necessary conditions for the subsequent propagation of the disease.

It remains, therefore, to be determined whether the limits of temperature and of altitude within which the *C. mosquito* is able to exert its functions, agree with those which are known to limit the propagation of yellow fever. The following simple experiments appear conclusive on these points:

1. Let a female *C. mosquito*, of medium size, be placed in a test-tube with a thermometer passing through the cotton-plug, and the tube dipped in water, the temperature of which is gradually lowered by the addition of ice and salt. The following effects will be observed:

Between 66° and 60° F., the insect is benumbed, scarcely moving, sometimes falling to one side in a state of apparent death.

Between 60° and 32° F., apparent death more pronounced.

If the water be allowed to return to its former temperature:

Between 60° and 65° F., the insect shows signs of life.

Between 65° and 68° F., it is able to walk and fly.

Above 77° F., it recovers its former agility, but is at first unable to bite; indeed, if the cooling has reached 32° F., or below, the insect generally dies within a short time.

The larger varieties seem, however, to bear low temperatures better than the small, and a difference is observed according as the change is effected more or less rapidly.

2. In order to test the limits of heat, let a test-tube, similarly disposed, with a thermometer and live mosquito, be suspended inside of a large empty flask, standing in a basin of hot water. The following effects will be noted:

Between 95° and 100° F., the insect appears uncomfortable.

Between 102° and 105° F., remains motionless in apparent death, but is apt to recover and to sting again when restored to a normal temperature.

From 105° to 110° F., apparent or actual death; the insect, if it does revive, not being able to sting again, and generally dying within a few hours.

3. As regards barometric pressures, the experiment would best be tried in such localities as Vera Cruz, Orizava, and Mexico, or in Rio Janeiro and the heights near it, but, failing that resource, I have contrived the following plan:

A female *C. mosquito* is placed in an empty bottle connected with an aneroid barometer, and a suction flask raised to a proper height:

At rarefied pressures corresponding to 2000 or 3000 feet, the

insect becomes at first unable to fly, but if withdrawn will bite and draw blood after a while.

At rarefied pressures corresponding to 4000 or 6000 feet, the the general effects are more marked, but the insect does not die, and seems even to (p. 401) get accustomed to the new state of things; but when withdrawn continues weak, and unable to sting for several hours.

We are thereby led to infer that the *C. mosquito*, when suddenly transferred to heights above 3000 or 4000 feet, must find it difficult to exert its functions, and that it would never, of its own accord, seek elevations which render its flight difficult. This conclusion agrees, moreover, with the remarks of Baron von Humboldt, who carefully observed the mosquitoes of Central America.

From the above experiments it is inferred that the limits of functional activity for the *C. mosquito* are: as regards temperature, between 60° and 100° F., the insect reviving, however, after having been chilled to near 32° F., or warmed to 105° F.; as regards altitude, from the level of the sea to 3000 or 4000 feet. Now the limits which most observers assign to the propagation of yellow fever are temperatures ranging from 60° F. to 90° F. ("Barton's Reports," 1852, pp. xiii. and 283); a general temperature of 32° F. having, however, proved ineffectual to prevent the recurrence of the disease (in the case of the "Plymouth"), when a tropical temperature was produced. As regards altitudes, the highest limit at which it has been observed seems to be 4000 feet above the level of the sea.

Before dismissing the subject under consideration, I must add that the mosquito finds within the precincts of a dwelling all the requirements for its development, growth, and reproduction; dark corners to hide in, stagnant water in which to lay its eggs and to develop its larvae, and substances for the female insect to feed on, being the principal conditions. A forgotten tub, or pool of stagnant water in a back yard or garden, is often chosen by the insects as a place of rendezvous where they congregate and lay

their eggs; the larvae, in the meantime, going through their successive stages of development. The mother insect when about to die, has been observed to resort to the water where its larvae are growing, its cadaver remaining floating upon the liquid surface. The nocturnal species will naturally lead a more stationary existence than the diurnal; for the latter, in trying to sting during the busy hours of the day, will often have to follow its intended victim from house to house, returning again and again after being driven off, until it succeeds in planting its sting and filling with blood. Wherever the bite happens to have been successful, there the mosquito will, in all likelihood, take up its quarters; it will develop a new brood and continue to sting all that come in its way, unless again led off by a chance peregrination.

Before relating the following six cases of experimental yellow fever, it will be proper to explain the general principles by which I was guided, and the process which I have followed in my inoculations.

The general disposition of the *C. mosquito's* sting has already been described, but for our present purpose it may be regarded as a slender (p. 402) hollow needle from $\frac{1}{30}$ to $\frac{1}{40}$ mm. broad and 2 mm. long, with its sides roughened by a series of transverse ridges and its point armed with teeth. This needle penetrates through the skin until it reaches one of the capillaries of the corium, generally to the depth of 1 to 2 mm., remains in position during a space of from one to five minutes, and, after being withdrawn, will continue protected by its sheath against external agents until the insect's next bite. I have been able to prove that the sting often retains spores of microscopical fungi, which may be made to develop by keeping the proboscis in a sterilized cell, and I once found upon the side of the sting a finely developed bunch of spores like those observed in yellow fever blood cultures by Dr. Sternberg (*Bacteria*, 2d edition, p. 426), and classified as "*Penicillium*;" whence it is to be inferred that it may likewise retain upon its outer surface or inside of its sheath, such minute disease-germs as are generally believed to occasion most of the zymotic diseases. If so, the sting of the mosquito having been impregnated with the animal juices during

the operation of stinging, may constitute an appropriate soil for the preservation or even for the culture of those germs; might it not, indeed, be the "intermediate host" necessary for some phase of their development?¹

For the purpose of carrying into effect this novel inoculation, my plan has been to catch a female mosquito while in the act of stinging and before it has filled, by inverting an empty phial or test-tube over it and closing the mouth of the phial with a plug of cotton-wool. The insect is thus in readiness to renew its bite as soon as it has become accustomed to its place of confinement. Indeed, it will die of inanition if not allowed to do so in the course of a few hours (four to twelve in summer). The captive is then taken to a confirmed case of yellow fever, and the tube being inverted and the cotton plug carefully removed over the bare surface of the patient's arm or hand, the insect is allowed to fill at leisure with the tainted blood, and the plug reinserted. After this blood has been digested, generally between the second and fourth day, the mosquito is applied in the same manner to the arm of a subject liable to the disease, and then allowed again to fill itself completely. This is the inoculation; and when successful, at the end of from five to twenty-two days incubation, the first symptoms of mild yellow fever will manifest themselves in the inoculated subject.

The process, as above described, is simple enough, but it must be observed that in order to obtain available results several conditions are necessary. A case of yellow fever must be at hand at the period most favorable for the transplantation of the virus, which, according to my (p. 403) experiments, seems to be from the third to the sixth day. A liable subject must be found willing to submit to the process, supposed to be free from previous infection, and likewise willing to keep clear from infected places during the incubation, yet within easy reach of observation.

The nocturnal species of mosquito can easily be procured, but,

¹ In resolving to experiment upon human subjects, I relied upon the inference that the quantity of virus carried by a single sting must be a minimum dose, capable of producing only the mildest forms of the disease ever observed in nature, and that a number of such bites would be necessary to occasion a dangerous attack.

as before stated, I have never succeeded in making that particular kind sting more than once; whereas, the diurnal, which is the only one that I have experimented with, does not generally come in swarms, but singly, or in small numbers, making but little noise, and its bite is usually unfelt, at least by the acclimated.

These requisites, so difficult to be obtained by one whose leisure hours, in the midst of an active professional life, are necessarily limited, will account for the small number of my experiments, some twenty-four individuals only having been inoculated by me since June, 1881. Of this number only one has died of yellow fever; he had been inoculated in November, 1883, without any visible result, and was attacked, after severe exposure, in June, 1884, with a malignant form of yellow fever (it is the second case of the series referred to elsewhere as instances of contagion). Of the remaining twenty-three, two left the country, or were lost sight of the first summer after inoculation, the rest having remained under observation during periods ranging between one and four full summers in the city of Havana. Six of these inoculations were followed within the ordinary limits of yellow fever incubation (five to twenty-two days), by an attack of fever, the exact counterpart of mild attacks of yellow fever, of which I have kept careful notes, and which were proved by subsequent observation to have conferred immunity. Eleven inoculations, though not followed by any morbid manifestation, at the end of several months a mild attack of yellow fever (without albuminuria) was observed.

These figures are not considered, from a statistical point of view, to afford any definite clue either in favor of or against the prophylactic value of my inoculations when not followed by a mild attack of the disease, and it is rather upon the circumstances attending my six successful inoculations that I rely in order to prove the aptitude of the *C. mosquito* for transmitting yellow fever. If this be once admitted, it must follow that the disease is actually so transmitted, since it must constantly happen, in a place like Havana, that unacclimated subjects (p. 404) are stung by mosquitoes which have previously bitten yellow fever patients.

My first inoculations by means of mosquitoes were performed under the following circumstances: A group of twenty unacclimated soldiers, who were quartered on the heights of the Cabanas, on the other side of the bay, were picked out for my observations, and were only allowed to cross the bay in batches of four or five on the days they were sent to my office, where I tried their blood for hematimetric purposes. Five of the group were inoculated by me at different dates between the 29th of June and the end of August, 1881. The first three were followed, at the end of five or fourteen days' incubation, by an attack of fever of several days' duration, diagnosticated by the attending physicians at the military hospital as "regular yellow fever" in the first case, and "abortive yellow fever" in the two others. The fourth inoculated soldier suffered only from continued headache, and, on the fifteenth day after the inoculation, came to my office with slight fever (temperature 100.7° F., pulse 100), but was not laid up. The fifth did not return to my office. I was informed that he had felt poorly a few days after the inoculation, but was not laid up. I have been able to trace the history of these five cases until the beginning of last year. None of them had been reported, up to that date, as subsequently attacked with yellow fever. Of the remaining fifteen soldiers of the group, upon whom the inoculation *was not performed*, none were attacked with yellow fever during the period of my observation, June 28 to September, 1881.

CASE I—On the 30th of June, 1881, one of the soldiers of the above group (F. B.), twenty-two years of age, three months in Havana, having had previously some attacks of intermittent fever, was inoculated by means of a mosquito which had bitten, two days before (June 28th), a patient in the fourth day of yellow fever and who died thirty-six hours later.

July 14. The inoculated soldier was taken sick and went to the Military Hospital, where I was only able to see him on the 16th (third day of his illness). I found him with slight fever, slight yellowish tinge of conjunctivae, pains of invasion almost disappeared; the urine gave distinct evidence of albumen with heat and with nitric acid, not having presented any in the morn-

ing. The clinical report of the attending physician, together with my own observation, gave the following result.

1st day, July 14. Invasion preceded by a few days of discomfort.

2d day. Morning: Temp. 101.8° F.; pulse 92; resp. 28; face and eyes injected; intense headache; slight epigastralgia; pains in the spine; tongue coated; no vomiting or other remarkable symptoms. Treatment: Ipecacuanha four grammes in four doses; cream of tartar lemonade; absolute diet. Evening: Temp. 100.4° F.; pulse 88; resp. 26; headache less intense. Night: Intense thirst; urine scanty.

3d day. Morning: Temp. 99.6° F.; pulse 72; resp. 34, skin pale; slight yellowness of conjunctivae; congested gums; epigastralgia; no nausea; no albumen in the urine. Evening: Albumen detected in the urine. Night: Same condition; insomnia. Treatment: One gramme of sulphate (p. 405) of quinine in ten doses; cream of tartar lemonade; mustard plasters to the extremities.

4th day. Morning: Temp. 98.9° F.; pulse 72; resp. 34; no headache; some appetite; gums give a little blood on compression; urine treated by heat and nitric acid, gives a more abundant precipitate of albumen. Evening: Normal temperature and pulse.

5th day. Temp. 98.9° F.; pulse 78; respiration normal; slight jaundice; urine contains albumen.

6th day. Convalescent; urine not examined; broth allowed.

7th day. Continues well.

12th day. Cured.

The distinct evidence of albumen in the urine, notwithstanding the mildness of the fever and general symptoms, leaves no doubt regarding the diagnosis, which was unhesitatingly reported as "regular yellow fever."

CASE II.—Another soldier of the group (A. L. C.), seventeen years of age, three months in Havana, was stung on the 22d of July, 1881, by a mosquito which had bitten, on the 16th, a bad case of yellow fever (in fifth day of his illness), and on the 20th had been made to sting my own hand.

July 27. Five days after the inoculation, this soldier entered

the Military Hospital with an attack of fever, which was qualified as "abortive yellow fever." When seen by me on the 31st (fifth day of his illness), there was scarcely any fever, and the urine contained no albumen. I was unable to procure the clinical notes of this case.

This observation would tend to prove that an infected mosquito does not always lose its virulence by an intermediate bite. This is not always the case, however, for on a subsequent occasion, having inoculated with a mosquito which had bitten two yellow fever patients, a person who seems thereby to have acquired subsequent immunity, the same insect was afterward made to sting a second non-acclimated person, who had a severe attack of yellow fever six months later, from which he fortunately recovered. This case has not been included among my regular inoculations, being considered a distinct experiment.

CASE III.—A third soldier (D. L. F.), twenty years of age, and six months in Havana, was inoculated on the 31st of July, 1881, with a mosquito which had bitten, two days before, a fatal case of yellow fever in third day of the disease. On the 5th of August (five days after the inoculation) the soldier came to my office, presenting temp. 39.6° , and pulse 110. He was at once sent to the Military Hospital, where the following clinical record was taken:

1st day, August 5. Evening: Temp. 103.2° F.; pulse 112; intense headache; slight epigastralgia; flushed countenance; intense thirst. Treatment: Valerianate of quinine two grammes in twenty pills; mustard plasters to the extremities; cold applications to the forehead.

2d day. Morning: Temp. 100.7° F.; pulse 72; resp. 28; the pains have lessened; some nausea; subicteric tint; urine pretty abundant, contains no albumen. Evening: Temp. 101.8° F.; pulse 88. Night: Temp. 100.7° F.; pulse 82; insomnia.

(p. 406) *3d day.* Morning: Temp. 99.6° F.; pulse 76; perspiration; no pains. Evening: Temp. 100° F.; pulse 80; restlessness.

4th day. Apyrexia.

The diagnosis, as stated in the clinical report, was "abortive yellow fever."

The following year (1882) my attention was principally devoted to the observation of mild forms of yellow fever, in order to collect reliable data available for the appreciation of my experimental cases. In 1883, however, I resumed my experiments, obtaining three successful inoculations, one of which (Case V.) is particularly worthy of notice.

CASE IV.—A Spaniard (J. B.), employed as a servingman to my friend Dr. Delgado, twenty-five years of age, nine months in Havana, having never been ill since his arrival, was inoculated on the 22d of June, 1883, by two mosquitoes, which had both bitten, two days before, a fatal case of yellow fever in the sixth day of his illness.

July 9th (seventeen days after the double inoculation), J. B. was taken ill with symptoms of yellow fever. The following morning an emetic was administered, followed by a dose of castor oil; no other medicine being given in the course of the illness, and absolute diet maintained until the sixth day, only water being allowed.

2d day. Morning: Temp. 101.3° F.; pulse 80; face flushed; pains in the loins. Evening: Temp. 101.8° F.

3d day. Morning: Temp. 100.4° F.; pulse 70; no albumen in the urine. Evening: Temp. 101.8° F.; face less flushed; straw color of the conjunctiva; intense thirst; anorexia.

4th day. Morning: Temp. 99.5° F.; pulse 68; no albumen. Evening: Temp. 101.3° F.; pulse 70.

5th day. Morning: Temp. 100.4° F.; pulse 68; no albumen; conjunctivae yellowish; gums do not bleed on pressure.

6th day. Morning: Temp. 101.4° F.; pulse 72. Midday: Temp. 103.1° F.; pulse 72. Evening: Temp. 103.2° F.; pulse 70.

7th day. Morning: Temp. 98° F.; pulse 54; yellowish tinge on the forehead; no pains; has perspired freely in the night; milk allowed. Evening: Temp. 98.6° F.; pulse 52; appetite returning; rapid convalescence.

The general type of the fever, with remission on the fourth day, and defervescence on the seventh, bears a strong resemblance to some forms of natural yellow fever that I have observed. The patient has since remained protected.

The following case is remarkable from the circumstance that most of the conditions were fulfilled that can well be secured in the vicinity of Havana, in order to avoid the chances of independent infection from other sources besides the inoculation. The place selected for the experiment was the same country residence or "Quinta" rented by the Jesuit Fathers since 1872, near the "Quemados de Marianao," to which Dr. Stanford E. Chaillé has alluded in his remarkable report as President of the Yellow Fever Commission which visited Havana in 1879 (*Annual Report of the National Board of Health*, Washington, 1880, p. 276 (p. 407)). In the course of eleven years (1872-1883), the only case of yellow fever developed among the many liable subjects who had spent their summer vacations at this place, during their stay, occurred in 1880 in a young priest who had been going backward and forward to Havana during the previous fortnight, and who was attacked with the disease during his last visit to the city, where he remained and died. It is more than likely that he had contracted the infection in town, and not at the Quinta.

Toward the end of June, 1883, several young priests and a servant, all unacclimated and having arrived from Spain the previous autumn, happened to be staying at this country-place, and I availed myself of their willingness to submit to my inoculation experiments.

CASE V.—P. U., one of the unacclimated priests, a young man of spare habit, having gone to the "Quinta" toward the end of June, 1883, did not again visit the city nor the neighboring town of Marianao until the following September. On the 15th of July a first unsuccessful attempt was made with a mosquito contaminated from a case in the seventh day of yellow fever; a full month was then allowed to elapse before a second attempt on the same person.

August 18, 1883, P. U. was inoculated with a mosquito which had bitten on the 13th and 16th two separate cases of yellow fever, each in the sixth day of their illness.

On the 26th of August, eight days after inoculation, P. U. was taken ill about 8 A.M. with headache, pains in the loins, and fever (temp. 100.7° F.). I saw him at 4 P. M. and from that time followed the case, keeping accurate notes of the symptoms.

1st day. 4 P. M., felt very poorly, complained of headache and pains in the loins and calves; face flushed and covered with perspiration; eyes injected; was sent to bed, and after a while presented: Temp. 102.2° F.; pulse 100, dicrotic. Treatment: Castor oil with lime juice. Night: Temp. 102.3° F.; pulse 104; vomited five or six times through the night and had several passages; thirst; eyes injected.

2d day. Morning: Temp. 101.3° F.; pulse 88; resp. 20; eyes injected, without yellow tinge; urine natural in appearance. Evening: Temp. 101.4° F.; pulse 90; resp. 30; somewhat drowsy; urine less copious than usual, acid reaction, not affected by boiling. Treatment: Hyposulphite of soda; boiled orangeade for common drink.

3d day. Morning: Temp. 101.8° F.; pulse 80; resp. 27; urine contains no albumen; restless night, insomnia; tongue white; thirst; face less flushed. Evening: Temp. 101.8° F.; pulse 84; resp. 26; subicteric tinge of conjunctivae. Same treatment.

4th day. Morning: Temp. 100.4° F.; pulse 60; resp. 27; subicteric tinge more marked; the pains have ceased; urine scanty, contains biliverdine, but no albumen; the gums bleed on pressure. Treatment: Chlorate of potash. Evening: Temp. 101.4° F.; pulse 80; restlessness; urine scanty, no albumen; thirst; anorexia.

5th day. Morning: Temp. 101.1° F.; pulse 76; resp. 29. Evening: Temp. 101.8° F.; pulse 83. Night: During a thunderstorm became very nervous; ten hours without passing urine; urine presents traces of albumen. Treatment: Morphia syrup.

(p. 408) *6th day.* Morning: Temp. 101.8° F.; pulse 72; urine not altered by ebullition; quiet night; expectorated some bloody sputa. Broth allowed. Evening: Temp. 100.7° F.; pulse 75.

7th day. Morning: Temp. 99.6° F.; pulse 62; resp. 20; subic-

teric tint of conjunctivae; some bloody sputa; gums bleed on pressure; urine scanty, no albumen. Evening: Temp. 98.9° F.; pulse 57.

8th day. Morning: Temp. 98.7° F.; pulse 58; subicteric tint of conjunctivae.

It is worthy of notice that this patient in his normal condition presented a *polyuria insipida*, amounting to over two litres per day; the secretion becoming immediately reduced from the invasion of the attack.

The patient spent two summers in the city after this attack, visiting cases of yellow fever, and having witnessed two severe ones in the town-college where he resided, without experiencing any inconvenience.

CASE VI.—The unacclimated servant before mentioned, who was staying at the Jesuits' "Quinta" with the preceding case, and upon whom a first unsuccessful attempt had also been made on the 16th of July, was again inoculated on the same day as P. U.

August 18. This servant (J. S.) was stung by a mosquito which had bitten, three days before, one of the patients of yellow fever from whom the previous case was produced. J. S. remained at the "Quinta" until September 3d, at which date he had to return to the college in town. He was taken ill on the 9th and went into a private hospital, where I was able, with Dr. Delgado's assistance, to follow up the case.

1st day. Twenty-two days after the inoculation, taken ill in the evening, with fever, headache, and pains in the loins.

2d day. Midday: Temp. 103.1° F.; pulse 94; copious perspiration; headache; pains in the loins; eyes injected; tongue coated. Evening: Temp. 103.2° F.; pulse 96; resp. 24; urine acid, not precipitated by boiling.

3d day. Afternoon: Temp. 100.4° F.; pulse 84; resp. 20; urine acid, gives a distinct precipitate on being heated to the boiling point; tongue coated; face less flushed; thirst; anorexia.

4th day. Afternoon: Temp. 99.8° F.; pulse 66; resp. 22; urine

not precipitated by heat nor by NO_2 ; subicteric tint of conjunctivae; thirst; anorexia.

5th day. Midday: Temp. 99.3°F. ; pulse 64; resp. 22; urine turbid, no albumen; appetite returning.

6th day. Afternoon: Temp. 99.8°F. ; pulse 64; resp. 22; broth allowed.

7th day. Temp. 99.3°F. ; pulse 56; resp. 22; some appetite; conjunctivae subicteric.

The fact that this person had returned to Havana six days before the attack, together with the long incubation of twenty-two days, leaves a doubt regarding the part that the inoculation may have had in the causation of the disease; but, on the other hand, the small number of yellow fever cases reported at that time in Havana, and the circumstance that newcomers are not often attacked so early as six days after (p. 409) their arrival in the city, have induced me to include this among my successful inoculations.

From the evidence adduced in the preceding pages, I conclude that while yellow fever is incapable of propagation by its own unaided efforts, it may be artificially communicated by inoculation, and only becomes epidemic when such inoculations can be verified by some external natural agent, such as the mosquito.

The history and etiology of yellow fever exclude from our consideration, as possible agents of transmission, other blood-sucking insects, such as fleas, etc., the habits and geographical distribution of which in no wise agree with the course of that disease: whereas, a careful study of the habits and natural history of the mosquito shows a remarkable agreement with the circumstances that favor or impede the transmission of yellow fever. So far as my information goes, this disease appears incapable of propagation wherever tropical mosquitoes do not or are not likely to exist, ceasing to be epidemic at the same limits of temperature and altitude which are incompatible with the functional activity of those insects; while, on the other hand, it spreads readily wherever they abound. From these considerations, taken in

connection with my successful attempts in producing experimental yellow fever by means of the mosquito's sting, it is to be inferred that these insects are the habitual agents of its transmission. It cannot be denied, however, that other such agents may and probably do occasionally occur, but not being endowed with the same facilities for rapid and extensive operation, their influence becomes insignificant as compared with the action of the Cuban culex.

